

## Psychiatric Briefs

---

### **Olanzapine-Exposed Pregnancies and Lactation: Early Experience**

Goldstein DJ, Corbin LA, Fung MC

Treatment of women with antipsychotic medication during pregnancy introduces the risk of prenatal exposure of the fetus to the medication. The authors examined the effects of in utero and lactation exposure to the atypical antipsychotic olanzapine in 23 prospectively identified pregnancies (i.e., identified before the outcome of pregnancy was known) and 11 retrospectively identified pregnancies (i.e., identified after delivery or abnormal result of a diagnostic procedure). Outcomes in the prospectively identified pregnancies were within the ranges identified in historical controls: spontaneous abortion occurred in 13%; stillbirth, in 5%; and prematurity, in 5%. No major malformations were identified. In the retrospectively identified group, no adverse effects were associated with olanzapine in the 2 infants exposed to the medication during lactation. Although the risk of complications was low in fetuses and infants exposed to olanzapine, the number of subjects in this study was small and the data in the literature on the presence of olanzapine in breast milk are lacking. The use of olanzapine during pregnancy and lactation should be limited to those situations in which the potential risk to the fetus or infant is outweighed by the potential benefit of treatment.

(*J Clin Psychopharmacol* 2000;20:399–403)

### **The Effects of Olanzapine in Reducing the Emergence of Psychosis Among Nursing Home Patients With Alzheimer's Disease**

Clark WS, Street JS, Feldman PD, et al.

**Background:** Elderly patients with Alzheimer's disease (AD) commonly exhibit psychotic symptoms, prompting clinicians to administer antipsychotics. This article compares the effects of olanzapine and placebo in the emergence of hallucinations or delusions in AD patients with symptoms of agitation/aggression but little or no psychotic symptomatology at baseline. **Method:** A multicenter, double-blind, placebo-controlled study was conducted in nursing home patients with AD according to DSM-IV criteria and symptoms of agitation/aggression and/or psychosis. Patients (N = 206) were randomly assigned to receive either placebo or fixed-dose olanzapine (5, 10, or 15 mg/day) for up to 6 weeks. This article analyzes data from a subgroup of patients (N = 165) with no or minimal delusions and/or hallucinations at baseline as measured by the Neuropsychiatric Inventory-Nursing Home Version (NPI/NH). Three subsets of patients were identified on the basis of their symptoms at baseline: those with no clinically significant hallucinations, those with no clinically

significant delusions, and those with no clinically significant delusions or hallucinations. **Results:** Of the patients without hallucinations or delusions at baseline (N = 75), the placebo-treated patients showed significantly greater development of these symptoms compared with olanzapine-treated patients overall (NPI/NH hallucinations + delusions mean change score, +2.73 vs. +0.27,  $p = .006$ ). Similarly, of the patients without baseline hallucinations (N = 153), the placebo-treated patients showed greater hallucinations score increases than did olanzapine-treated patients overall (+1.25 vs. +0.33,  $p = .026$ ), whereas patients without baseline delusions (N = 87) showed no significant treatment effects. Olanzapine had a favorable safety profile in each patient subset. **Conclusion:** These results suggest that, overall, olanzapine effectively attenuated emergence of psychosis in a short-term trial of patients with Alzheimer's disease.

(*J Clin Psychiatry* 2001;62:34–40)

### **Pathways to Housing: Supported Housing for Street-Dwelling Homeless Individuals With Psychiatric Disabilities**

Tsemberis S, Eisenberg RF

**Objective:** Up to 33% of homeless individuals have a mental illness, and the rate is even higher among street-dwelling homeless persons. Pathways to Housing is a supported housing program in New York City that deviates from traditional programs that help mentally ill homeless individuals obtain housing only after they have undergone treatment for their mental illness. This study sought to determine (1) whether street-dwelling homeless individuals with mental illness or substance addictions could secure and maintain an apartment of their own without first receiving treatment and (2) whether programs that require prior psychiatric treatment are associated with a greater housing retention rate than programs, such as the Pathways program, that provide housing without requiring initial treatment. **Methods:** Housing tenure for 242 individuals housed through the Pathways program between January 1993 and September 1997 was compared with tenure for 1600 individuals housed through the traditional step-by-step treatment approach during the same time period. **Results:** After 5 years, 88% of individuals housed through the Pathways program remained housed, compared with 47% of individuals in the comparison group. The between-group difference in housing tenure remained when variables such as dual diagnosis, gender, and ethnicity were controlled for. **Conclusions:** The success of the "housing first" Pathways model challenges currently held assumptions of the connection between psychiatric symptoms and ability to maintain housing and suggests that, given the opportunity and

needed supports, individuals with mental illnesses are capable of securing and maintaining housing.

(*Psychiatr Serv* 2000;51:487–493)

### Association of Schizophrenia With Low Maternal Body Mass Index, Small Size at Birth, and Thinness During Childhood

Wahlbeck K, Forsén T, Osmond C, et al.

**Background:** Research has suggested an association between early-life nutritional factors and subsequent development of schizophrenia. The aim of this study was to elucidate the effects of maternal body mass index (BMI), size at birth, and childhood growth on later risk for developing schizophrenia and related disorders. **Method:** The subject pool comprised 7086 individuals born at the Helsinki University Central Hospital (Helsinki, Finland) between 1924 and 1933 who were still living in Finland in 1971. Data on maternal height and weight during late pregnancy and infant length and weight were gathered from birth records, and data on children's height and weight from ages 6 and 16 years (measured twice per year) were taken from school records. Subjects were linked to the Finnish Hospital Discharge Register to identify cases of schizophrenia, schizophreniform disorder, or schizoaffective disorder. **Results:** A total of 114 individuals had received a diagnosis of schizophrenia or a related disorder. Risk for schizophrenia was increased in individuals whose mothers had low late-pregnancy BMI (odds ratio [OR] = 1.09 per kg/m<sup>2</sup>; 95% confidence interval [CI] = 1.02 to 1.17) and who themselves had low birth weight (OR = 1.48 per kg; 95% CI = 1.03 to 2.13), were shorter at birth (OR = 1.12 per cm; 95% CI = 1.03 to 1.22), and had a lower placental weight (OR = 1.22 per 100 g; 95% CI = 1.04 to 1.43). Individuals who later developed schizophrenia had below-average weight and BMI from ages 7 to 15 years. Regression analysis found that only lower BMI at age 7 years was an independent predictor of development of schizophrenia. **Conclusion:** Factors possibly related to fetal and childhood undernutrition are associated with a higher lifetime risk of schizophrenia.

(*Arch Gen Psychiatry* 2001;58:48–52)

### Gamma-Hydroxybutyrate (GHB): A Newer Drug of Abuse

O'Connell T, Kaye L, Plosay JJ III

A recent increase has occurred in the abuse of the illegal drug gamma-hydroxybutyrate (GHB) among both bodybuilders, who claim it builds muscle and metabolizes fat, and party attenders, who seek its purported euphoric effects. Because of its depressant and purported aphrodisiac effects, GHB has also been used as a "date rape" drug. Originally synthesized in 1960 as an analgesic and later marketed as a "growth hormone stimulator," GHB was banned in 1991 by the U.S. Food and Drug Administration because of adverse reactions following its use and was declared a schedule I drug in 2000. GHB can be highly toxic,

especially in doses that exceed those needed for intoxication, and its toxicity varies widely due to the heterogeneity in the street manufacturing of the drug. The central nervous system depressant effects of GHB render it deadly when combined with other depressants such as alcohol. The authors describe the clinical presentation of GHB and its associated adverse effects and the treatment options for individuals who have ingested GHB. Finally, the authors recommend that physicians take the lead in educating the public about the dangers associated with the use of this drug.

(*Am Fam Physician* 2000;62:2478–2482, 2483)

### Bupropion SR Reduces Periodic Limb Movements Associated With Arousals From Sleep in Depressed Patients With Periodic Limb Movement Disorder

Nofzinger EA, Fasiczka A, Berman S, et al.

**Background:** Antidepressant-induced periodic limb movement disorder (PLMD) may limit the tolerability of some antidepressant medications and interfere with treatment response. Given the role of dopamine in PLMD and the effects of bupropion sustained-release (SR) on central dopaminergic function, we hypothesized that bupropion SR would not be associated with antidepressant-induced PLMD. **Method:** In an expanded case-series design, we compared the effects of bupropion SR, after about 10 weeks of treatment, on measures of PLMD, depression, and sleep in 5 depressed (Research Diagnostic Criteria) patients who also met criteria for having pretreatment PLMD. Depression was measured using the Beck Depression Inventory and the Hamilton Rating Scale for Depression. Patients were considered to have PLMD if polysomnographic recordings showed > 5 periodic limb movements/hour of sleep that were associated with arousals from sleep. **Results:** Bupropion SR treatment was associated with a reduction in measures of PLMD and an improvement in depression. **Conclusion:** These results show that bupropion SR is not associated with antidepressant-induced PLMD. Rather, bupropion SR treatment reduces objective measures of PLMD in depressed patients with the disorder.

(*J Clin Psychiatry* 2000;61:858–862)

### Ambulance Personnel and Critical Incidents: Impact of Accident and Emergency Work on Mental Health and Emotional Well-Being

Alexander DA, Klein S

**Background:** Although ambulance personnel are often thought to have especially "hardy" personalities, they can be vulnerable to psychological disturbances after exposure to traumatic events. The aims of this study were to determine the association between regular exposure to traumatic incidents and the mental and emotional health of those exposed and to identify whether "hardiness" shielded individuals regularly exposed to critical incidents from psychopathology. **Method:** An anonymous questionnaire booklet was administered to 160 ambulance personnel

who performed accident and emergency duties at a Scottish regional ambulance service. The booklet included standardized measures including the 28-item General Health Questionnaire (GHQ-28, to measure general psychopathology), the Impact of Event Scale (posttraumatic symptoms), the Maslach Burnout Inventory, and the Hardiness Scale. **Results:** Of the 110 personnel who completed the booklet, 90 (82%) had experienced a traumatic event in the previous 6 months. Thirty-five subjects (32%) reported general psychopathology as measured by the GHQ-28, and one fourth to one third of subjects exposed to traumatic events reported depersonalization, emotional exhaustion, and/or low job satisfaction. Twenty-seven (30%) of the 90 subjects exposed to trauma had highly severe posttraumatic symptoms. Low job satisfaction, longer time in emergency work, shorter recovery time between traumatic incidents, and more frequent exposure to trauma were all associated with burnout. Subjects exposed to particularly disturbing events in the previous 6 months were more likely to experience burnout and develop psychopathology. Those with especially hardy personalities experienced less burnout. **Conclusions:** Overall, regular exposure to critical incidents seems to have a deleterious effect on the mental and emotional well-being of ambulance personnel.

(*Br J Psychiatry* 2001;178:76–81)

### Outcomes After Initial Receipt of Social Security Benefits Among Homeless Veterans With Mental Illness

Rosenheck RA, Dausey DJ, Frisman L, et al.

**Objective:** The aims of this study were to identify sociodemographic or health characteristics of homeless veterans that may predict which veterans would and would not be awarded disability payments and to determine whether receipt of disability payments affected the health status, quality of life, income, and spending of recipients. **Methods:** The study included a convenience sample of 280 homeless veterans with mental illness enrolled in the Social Security Administration–Department of Veterans Affairs (SSA-VA) Joint Outreach Initiative between 1992 and 1999. Patients completed a face-to-face interview immediately before and 3 months after being awarded or denied SSA payments. Sociodemographic characteristics, clinical status, and social adjustment were compared at both timepoints between veterans who did and those who did not receive disability payments. **Results:** A total of 173 veterans completed both interviews. Among those, baseline demographic and clinical characteristics did not differ between the 50 veterans who received benefits and the 123 who were denied benefits. After 3 months, beneficiaries showed a greater total income, overall spending (although not on alcohol or illegal drugs), and overall quality of life but less motivation to work compared with nonbeneficiaries. Beneficiaries and nonbeneficiaries did not differ on measures of psychiatric status and substance abuse. **Conclusions:** Receipt of disability payments is associated with improved quality of life, but not increased alcohol or drug use, among homeless veterans.

(*Psychiatr Serv* 2000;51:1549–1554)

### The Quality of Care for Depressive and Anxiety Disorders in the United States

Young AS, Klap R, Sherbourne CD, et al.

**Background:** Although research has estimated the overall quality of care for a variety of medical disorders across the United States, such estimates have been lacking for depressive and anxiety disorders, despite the prevalence of these disorders. This study estimated the likelihood of receiving care, the appropriateness of treatment, and factors that influence receipt of treatment in U.S. adults. **Methods:** Subjects were interviewed over the telephone during 1997 and 1998 as part of the HealthCare for Communities initiative. The probable presence of major depression, dysthymia, panic disorder, and generalized anxiety disorder was ascertained via a brief psychiatric interview, and respondents were asked to provide information on services and treatment received in the past 12 months. Treatment was deemed appropriate if it conformed to established treatment guidelines. **Results:** A total of 1636 respondents met criteria for at least 1 depressive or anxiety disorder. Of these individuals, 80.8% visited a primary care physician, of whom 19% received appropriate care (95% confidence interval [CI] = 16% to 23%). Of the 19.4% of respondents who visited a mental health specialist, 90% received appropriate care (95% CI = 85% to 94%). Receipt of appropriate care was not influenced by insurance and income; however, individuals who were black, male, less educated, and younger than 30 years or older than 59 years were less likely to receive appropriate care. **Conclusions:** Overall, appropriate treatment is not being received by most adults in the United States with probable depressive or anxiety disorders, and certain demographic factors render the likelihood of receipt of appropriate treatment even lower in subgroups of individuals.

(*Arch Gen Psychiatry* 2001;58:55–61)

### Divalproex Sodium in Substance Abusers With Mood Disorder

Albanese MJ, Clodfelter RC Jr., Khantzian EJ

**Background:** Substance abuse is a common comorbid illness in patients with mood disorders. Little has been written about the pharmacologic treatment of patients with affective lability and co-occurring substance abuse, however. The following report will describe clinical experience using divalproex sodium in substance-abusing patients with mood disorder. **Method:** Twenty patients admitted to an intermediate-care inpatient substance abuse program were diagnosed with comorbid mood disorder (according to DSM-IV criteria) and treated with divalproex sodium in an open-label, naturalistic trial with no blind. All patients were followed clinically and were assessed using the Clinical Global Impressions scale (CGI) and laboratory studies. **Results:** Seven patients referred while on divalproex treatment continued to exhibit improved mood. Eleven others had at least 1 week of follow-up, and 10 of these also showed improvement. In 13 cases, divalproex was used safely with other psychiatric medications. Two patients complained of slight tremor, 1 of whom was also taking fluoxetine. Fifteen of

17 patients in whom biochemistry and hematology laboratory studies were completed had unremarkable results; 2 other patients had pretreatment abnormalities, which worsened over the course of treatment. Mean plasma valproate level was 58.53 mg/mL. Mean length of follow-up was 38 days. Mean period of abstinence prior to starting medication was 48 days. Some patients reported decreased cravings, and, by self-report, all patients remained abstinent. **Conclusion:** This report suggests that divalproex sodium is efficacious and safe, both alone and in combination with other psychiatric medications, in treating substance-abusing patients with mood disorder.

(*J Clin Psychiatry* 2000;61:916–921)

### Adult ADHD: Evaluation and Treatment in Family Medicine

Searight HR, Burke JM, Rottnek F

Although up to one half of adults who had attention-deficit/hyperactivity disorder (ADHD) as children continue to experience ADHD symptoms, family physicians are often uncomfortable in evaluating and treating adults with this disorder. The defining symptoms of ADHD in adults (e.g., restlessness, inability to prioritize) differ subtly from those of ADHD in children; thus, the disorder can be difficult to diagnose in adults using established criteria, which were developed to identify childhood ADHD. Accurate diagnosis of ADHD in adults requires the collection of a substantial amount of data from patients, including treatment history, patient self-report of symptoms, and current mental status. Physicians must differentiate between ADHD and other psychiatric disorders that have a similar symptom profile—especially major depression and substance abuse or dependence—and recognize that ADHD is often comorbid with other psychiatric disorders. Psychostimulants are the most commonly prescribed medications for adults with ADHD, but treatment with antidepressants is increasing in frequency. Additionally, pharmacotherapy is enhanced by the incorporation of self-management strategies and psychotherapy.

(*Am Fam Physician* 2000;62:2077–2086, 2091–2092)

### Gabapentin in the Treatment of Cocaine Dependence: A Case Series

Myrick H, Henderson S, Brady KT, et al.

**Background:** Although multiple medications have been studied for the treatment of cocaine dependence, no medication has been shown to have a robust effect on craving and use. This pilot project was designed to evaluate the safety and tolerability of gabapentin in subjects with cocaine dependence. **Method:** Thirty cocaine-dependent subjects (DSM-IV criteria) were enrolled in an 8-week, open-label trial of 1200 mg/day of gabapentin in divided doses. Urine drug screens, subjective measures of craving, and cocaine use interviews were conducted at each weekly visit. **Results:** Baseline rating of amount and frequency of craving decreased significantly by week 8 (78% vs. 25% for amount,  $p = .000$ ; 74% vs. 23% for frequency,  $p = .004$ ). Posi-

tive urine drug screens for cocaine decreased from 86% at baseline to 29% at weeks 4 and 8. There were no reports of significant side effects or adverse events. **Conclusion:** This pilot study indicates that gabapentin is safe and well tolerated and may be beneficial in the treatment of cocaine dependence. A placebo-controlled trial would be of interest.

(*J Clin Psychiatry* 2001;62:19–23)

### Schizophrenia, Obesity, and Obstructive Sleep Apnea

Winkelman JW

**Background:** This study evaluated the risk factors for obstructive sleep apnea in psychiatric patients. **Method:** The subjects were 364 patients referred to a sleep disorders consultation service from an inpatient psychiatric hospital. Seventy-eight percent underwent polysomnographic testing. Rates of obstructive sleep apnea in different diagnostic groups (established by clinical DSM-III-R diagnosis) were retrospectively assessed.

**Results:** Logistic regression demonstrated significant independent effects of age ( $p = .046$ ), gender ( $p = .002$ ), body mass index ( $p < .001$ ), and chronic neuroleptic use ( $p = .012$ ) on the presence of obstructive sleep apnea (defined as more than 20 instances of apnea and/or hypopnea per hour of sleep). Patients with schizophrenia were significantly heavier and had higher rates of sleep apnea than did other psychiatric patients. **Conclusion:** Obesity, male gender, and chronic neuroleptic administration are risk factors for obstructive sleep apnea in psychiatric patients. Since patients with schizophrenia are often on long-term neuroleptic treatment, they may have high rates of obstructive sleep apnea, mediated via the weight gain produced by such medications. Overweight psychiatric patients and those on chronic neuroleptic treatment (e.g., patients with schizophrenia) should be evaluated for sleep apnea if signs and symptoms of this disorder are present.

(*J Clin Psychiatry* 2001;62:8–11)

### Melatonin in Medically Ill Patients With Insomnia: A Double-Blind, Placebo-Controlled Study

Andrade C, Srihari BS, Reddy KP, et al.

**Background:** It has been suggested that melatonin improves sleep functioning, but this possibility has not been studied in medical populations. **Method:** 33 medically ill persons with initial insomnia were randomly assigned to receive either melatonin ( $N = 18$ ) or placebo ( $N = 15$ ) in a flexible-dose regimen. Double-blind assessments of aspects of sleep functioning were obtained daily across the next 8 to 16 days. **Results:** The mean stable dose of melatonin was found to be 5.4 mg. Relative to placebo, melatonin significantly hastened sleep onset, improved quality and depth of sleep, and increased sleep duration without producing drowsiness, early-morning “hangover” symptoms, or daytime adverse effects ( $p < .05$ ). Melatonin also contributed to freshness in the morning and during the day and improved overall daytime functioning. Benefits were most apparent during the first week of treatment. **Conclusion:** Melatonin may be a useful



hypnotic for medically ill patients with initial insomnia, particularly those for whom conventional hypnotic drug therapy may be problematic.

(*J Clin Psychiatry* 2001;62:41–45)

### **Depression in Children and Adolescents**

*Son SE, Kirchner JT*

Physicians have become increasingly aware that depression and related disorders manifest in children. Despite this growing awareness and despite the fact that depression is common in children (2%) and adolescents (5% to 8%), depression often remains unrecognized and untreated in these age groups. The presentation of depression in children and adolescents ranges from simple sadness to depressive disorders of varying severity to full-blown major depressive disorder and bipolar disorder. The constraints of the managed care environment necessitate a tool for identifying depression in children and adolescents quickly and accurately, such as the parent-rated Pediatric Symptom

Checklist and other questionnaires. Of chief importance in diagnosing depression is taking into account any medical conditions with symptoms that mimic those of depression. Although evidence-based treatment of depressive illnesses in children and adolescents is limited, psychotherapy has been shown to be effective in treating milder forms of depression, whereas pharmacotherapy with antidepressants such as the (older) tricyclic antidepressants and the (newer) selective serotonin reuptake inhibitors is indicated for more severe illness. Patients with severe or treatment-refractory depression should be referred by primary care physicians to mental health professionals as soon as possible; indeed, close collaboration between primary care physicians and child psychiatrists, psychologists, counselors, and social workers is essential to ensure that all children with depression receive the highest quality of care. To benefit readers, the authors have included useful assessment tools in the article, including a patient information handout, the Pediatric Symptom Checklist, and a questionnaire to evaluate the psychosocial status of children and their families.

(*Am Fam Physician* 2000;62:2297–2308, 2311–2312)